# Program Overview

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# Vision

- *Accelerate* the application of knowledge derived from basic research into the clinical and/or public health setting with the goal of improving human health.

- *Create* opportunities to develop and apply novel approaches for the diagnosis, prognosis, prevention, and treatment/intervention of environmentally-influenced diseases.

# Interdisciplinary Goal

*Incorporate basic mechanistic and clinical studies to:*

- Identify the underlying physiological mechanisms in disease pathogenesis and progression

- Characterize disease phenotype

- Understand the environmental and endogenous factors that affect the distribution of disease in populations

- Assess individual risk of developing disease

- Apply the knowledge gained to develop therapeutic, diagnostic, prognostic, and preventative strategies

# Overcome Longstanding Barriers

**Barriers:**

The environmental component in human disease has been difficult to ascertain**:**

- low levels of exposure

- lack of precision in the methods to assess exposure over time,

- inability to characterize the attributable risk from multiple exposures

- lack of statistical and computational approaches to measure gene-environment or gene-environment-comorbidity interactions

**Potential Solution:**

**Incorporation of emerging tools** ('omics', nanotechnology, molecular imaging) **with a clinical research focus** offer opportunities to understand the underlying biology that confers variability in disease response and the influences of exposure.

# Research Scope

A DISCOVER Center must reflect an **integrated research enterprise** that will advance our understanding of how environmental stimuli interact with biological processes to either preserve health or cause disease.

- **Any human disease or dysfunction, provided adequate justification**

- **Any 'primary stressor' (chemical, physical or biological toxicant)**

  - Modulation of susceptibility by secondary modifiers (co-morbid disease/conditions, aging, diet, infectious disease, and/or idiosyncratic drug reactions)

  - For the purposes of this initiative proposals focusing solely on secondary modifiers, including but not limited to, smoking, alcohol, infectious agents or diet, in the absence of primary stressors, will not be considered responsive

# Suggested Themes

## Disease Process

- Characterize disease etiology, pathogenesis, or progression

- Identify  target gene-environment interactions and novel approaches to therapeutic intervention.

## Susceptibility

- Clarify the contribution of environmental and genetic variables in the risk of developing disease and the risk of disease progression.

- Identify secondary modulators of susceptibility to environmental exposures

## Intervention

- Stratify disease risk and target intervention to promote improved health at the individual or population level.

# Translational Outcomes

- Development of sensitive pre-clinical markers of exposure and biological response

- Development of novel therapeutic agents and/or diagnostic tools

- Development of biomarkers for disease phenotype, onset, severity or progression

- Application of biomarkers as prognostic indicators of human diseases as well as therapeutic efficacy

# Characteristics of a Center Program

- **Creates a Focal Point within the NIEHS portfolio for translational research**

- **Provides a source of knowledge, tools, and resources for reducing the burden of disease**

**One key factor is that the impact of the DISCOVER Program will extend beyond the particular scope of the individual Centers.**

# Administrative Eligibility Criteria

- Applicant Institution must be **Domestic, Public or Private Institution** (foreign and for-profit consortia agreements are acceptable)

- Clearly stated justification of a **focus on human disease** in which **environmental factors are known or expected to influence the disease process**

- **Center Director**
  - provides overall leadership (minimum 15% effort)

- **Lead physician scientist**
  - ensure communication and translation across the research projects (15% effort)

- **Four integrated research projects (Project Leader – 20% effort)**
  - two "patient-oriented clinical/public health" research projects
  - two mechanistically-driven "basic" research projects
  - additional projects are encouraged.

- **Administrative Core**
  - external advisory committee
  - support product development to translate knowledge & resources

- **Facility Cores (optional)**

# Scientific Eligibility Criteria

## What is the definition of 'clinical' research for the DISCOVER Program?

- Patient-oriented clinical research conducted with human subjects, or research on the causes and consequences of disease in human populations involving material of human origin (such as tissue or specimens) and for which an investigator or colleague directly interacts with human subjects in an outpatient or inpatient setting to clarify a problem in human physiology, pathophysiology or disease

- Development of new clinically-based technologies, therapeutic interventions, or clinical trials

- Epidemiologic and behavioral studies in humans. Such studies are appropriate to the DISCOVER Centers in cases where the primary focus is on a specific disease.

- Any epidemiologic study or clinical trial supported by a DISCOVER Center must be limited to projects that can be completed within the five year timeframe of the Center and must be well justified within the disease/dysfunction theme of the overall Center application.

**Applicants must indicate in the application (Section II, Program Introduction) which projects are to be considered 'mechanistically driven' and which are to be considered 'patient-oriented/clinical.' These definitions are not mutually exclusive, a project may be mechanistically driven patient oriented research.**